Original Article

Diagnostic Value of the Modified Limb Lead System in Localizing the Origin of Outflow PVCs

Farzad Kamali[3], MD; Hamidreza Fallahabadi[1*], MD; Farzaneh Karamitanha[2], MD; Zahra Emkanjoo[3], MD; Majid Haghjoo[4], MD; Abolfath Alizadeh Diz[3], MD; Amirfarjam Fazelifar[3], MD; Shabnam Madadi[3], MD; Bita Jahangiri[3], MS

ABSTRACT

Background: The most common subgroup of premature ventricular contractions (PVCs) is the idiopathic outflow tract premature ventricular contraction (IOT-PVC). The radiofrequency catheter ablation of PVCs is the choice of treatment in drug-resistant or intolerant patients. There are many different ways to localize PVC origins, some of which pose a challenge. We hypothesized that changing limb electrode locations can help us localize IOT-PVCs.

Methods: This cross-sectional study was done in Rajaie Cardiovascular Medical and Research Center, Tehran, Iran, from 2019 through 2020. In all patients, in addition to surface electrography, 3 limb electrodes were placed at 3 spaces: right parasternal at the second intercostal space, left parasternal at the second intercostal space, and the tip of the left scapula. Three new vectors were achieved, which were then compared with the same-named limb vectors.

Results: The study population consisted of 102 patients. The voltage of the R and S waves of PVCs were compared in modified and conventional leads. All the formulas used had a statistically significant relationship (P<0.007) with the origin of PVCs other than I_{MR}/I_{CR} and I_{MR-S}/I_{CR-S}.

Conclusions: Comparison of the R and S waves of PVCs in modified lead II and III with the same-named conventional leads can yield the best results to estimate the origin of PVCs. The most useful formulas concerning sensitivity and specificity are II_{MR}/II_{CR} and III_{MR}/III_{CR}. The absence of notching at modified lead II can be a predictor of successful PVC ablation. ***(Iranian Heart Journal 2022; 23(4): 29-37)***

KEYWORDS: Outflow PVC, PVC location, Diagnostic value

[1] Department of Cardiology, Mousavi Hospital, Zanjan University of Medical Sciences, Zanjan, IR Iran.
[2] Department of Community Medicine, School Medicine, Zanjan University of Medical Sciences, Zanjan, IR Iran.
[3] Department of Cardiac Electrophysiology, Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, IR Iran.
[4] Department of Pacemaker and Electrophysiology, Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, IR Iran.

***Corresponding Author:** Hamidreza Fallahabadi, MD; Department of Cardiology, Mousavi Hospital, Zanjan University of Medical Sciences, Zanjan, IR Iran.
Email: fallah.hamidreza@yahoo.com **Tel:** +982433770801

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Early depolarization of the ventricular myocardium can result in arrhythmias called "premature ventricular contractions (PVCs)".[1] One of the most common arrhythmias in the world is the idiopathic PVC, with most patients complaining of PVC-associated symptoms like dyspnea and palpitations.[2,3] The most frequent subgroup of PVCs is the idiopathic outflow tract premature ventricular contraction (IOT-PVC).[4] IOT-PVCs mainly occur in the young and middle-aged populations without apparent structural and ischemic heart diseases. These PVCs are commonly considered benign and often treated with antiarrhythmic drugs. Nonetheless, radiofrequency catheter ablation (RFCA) is the choice of treatment in the following patients: 1) patients with frequent and long-standing IOT-PVCs, which are thought to be the etiology of tachycardia-induced cardiomyopathy; 2) patients with symptomatic IOT-PVCs resistant to antiarrhythmic drugs therapy; and 3) patients suffering from the side effects and proarrhythmic effects of antiarrhythmic drugs. RFCA could simultaneously identify the origin sites of PVCs and treat them.[5] Previous to catheter ablation, it is preferable to estimate the origin of the PVC noninvasively, which can result in shortening the duration of the procedure and decreasing complications.[6]

Surface 12-lead electrocardiography (ECG) can guide the determination of the PVC origin and the selection of the optimal approach and the access site (arterial or venous) for catheter ablation. PVCs originating from the right ventricular outflow tract (RVOT) have the following characteristics: an inferior frontal plane axis (R or RR′ morphology in leads II/III/aVF and a QS morphology in leads aVL/aVR) and a left bundle branch block (LBBB) shape with a precordial R/S transition at lead V_3 or later.[7,8] The 12-lead ECG of the left ventricular outflow tract (LVOT) originating PVCs shows a similar inferior frontal plane axis with an LBBB pattern and a precordial R/S transition at lead V_3 or earlier or with a right bundle branch block configuration and a precordial R/S transition at lead V_1.[9,10] Lead V_3 is a gray zone in which PVCs originating from the RVOT or the LVOT can have a precordial R/S transition.

Yoshida et al[11] evaluated 207 patients to localize the source of ventricular arrhythmias and introduced the V2S/V3R index. The authors concluded that the index with a cutoff value of 1.5 or less could predict LVOT origins with 89% sensitivity and 94% specificity. Xie et al[12] showed that an R-wave amplitude of 0.1 mv or greater in lead I could help ablate arrhythmias from the aortic sinuses of Valsalva or the LV endocardium with 75% sensitivity and 98.2% specificity.

Research has shown that IOT-PVCs have their respective 12-lead ECG characteristics.[13-15] Nevertheless, many of these computational algorithms are not only complicated and inconvenient in clinical practice but also have overlaps, rendering PVC localization difficult.

Concerning the cardiac anatomy and topography, the RVOT is close to the anterior chest wall and is, thus, considered an anterior structure. Additionally, the LVOT is posterior to the RVOT and is, hence, considered a posterior structure. Accordingly, we hypothesized that changing the locations of limb electrodes could assist us in predicting PVC origins more easily and provide us with a better understanding of PVC origins.

METHODS

The present cross-sectional study, performed in Rajaie Cardiovascular Medical and Research Center, Tehran, Iran, from 2019 through 2020 recruited all patients aged at least 18 years at the electrophysiology laboratory with a symptomatic inferior axis idiopathic PVC diagnosis with the following characteristics during a 1-year period: 1) patients intolerant to antiarrhythmic drugs, 2) patients resistant to antiarrhythmic drugs, and 3) patients with PVC-related cardiomyopathy.

Patients with a history of structural, ischemic, or congenital heart diseases were excluded from this study. Also excluded were patients with unsuccessful RF ablation procedures.

Previous to ablation, transthoracic echocardiography was done, and the left ventricular ejection fraction (LVEF) was measured by a cardiologist blinded to the study. Twelve-lead conventional surface ECGs were taken before ablation. Thereafter, the positions of limb electrodes were changed as follows: 1) The right arm electrode was attached to the second right parasternal intercostal space (electrode 1). 2) The left arm electrode was attached to the second left parasternal intercostal space (electrode 2). 3) The left arm electrode was attached to the second left parasternal intercostal space (electrode 3) (Fig. 1). With this method of limb electrode placement, 3 vectors were achieved. We called these modified vectors "I_M", "II_M", and "III_M", respectively.

The vector directions were as follows: I_M – electrode 1 as the negative pole and electrode 2 as the positive pole, II_M – electrode 1 as the negative pole and electrode 3 as the positive pole, and III_M – electrode 2 as the negative pole and electrode 3 as the positive pole (Fig. 1). Thereafter, the taken ECGs were analyzed by 2 cardiologists. If there was any discrepancy between the findings, the opinion of another cardiologist was sought.

To achieve homogeneity in the interpretation and comparison of PVCs in the leads, we considered 3 factors concerning every PVC in the modified and comparable conventional leads (Ic, IIc, and, IIIc). For instance, the positive portion of a PVC in modified lead I (R wave) was named "I_{MR}", and the negative portion (S wave) was named "I_{MS}" (Fig. 2). In conventional lead I, comparable portions were named "I_{CR}" and "I_{CS}", respectively. If a PVC had 2 R waves or S waves, the mean of the R waves or S waves was measured. In addition, the presence or absence of notching in these leads was assessed. Notching was defined as the presence of any positive or negative deflection in the ascending or descending portion of a PVC that did not meet the baseline. Thereafter, we measured the voltages of the R wave and S wave and measured the difference between these 2 modified and conventional leads. To determine voltage changes, we calculated the proportion of the R and S waves of PVCs in the modified and conventional leads (Fig. 3). We also presented simple formulas that compared the differences and proportions of the R and S waves (PVCs) in the modified and conventional leads using the formula I_{MR-IMS}/I_{CR-ICS}. After intracardiac mapping with the precise NavX system and ablation, the findings were compared with the intracardiac mapping diagnosis as the gold standard. For PVC ablation, activation mapping and pace mapping were performed to localize the PVC focus. RF ablation was performed using the guidance of fluoroscopy and with irrigated and non-irrigated catheters (ThermoCool SmartTouch, Biosense-Webster) targeting the areas of the earliest presystolic ventricular activation and 12/12 pace matches. Unsuccessful ablation procedures were excluded from this study. PVCs that were ablated successfully at the RVOT (the septal or free wall) or the LVOT (the aortic sinus of Valsalva and the infra-valvular area) were included in this study.

Statistical Analysis

Data analysis was performed using the SPSS software, version 23. After the assessment of the normality of variables with the Kolmogorov–Smirnov test, continuous variables were presented as the mean and the standard deviation and were compared using the Student *t* test. A receiver operating characteristic (ROC) curve was used for sensitivity and specificity analyses to calculate the area under the curve (AUC). A *P* value of less than 0.05 was considered statistically significant. Informed consent was taken from all the patients included in this study.

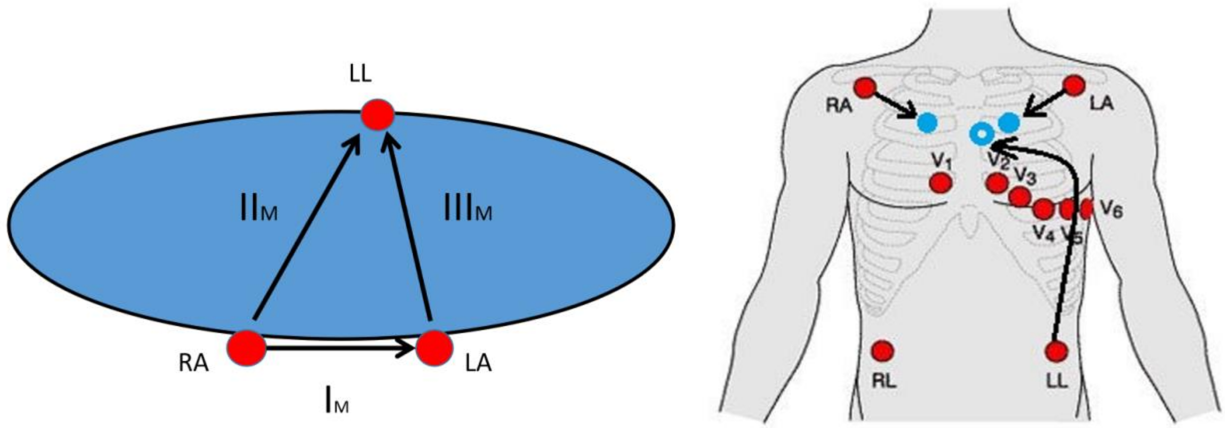

Figure 1: Modified limb electrode placement is illustrated herein. The right arm electrode is attached to the second right parasternal intercostal space, the left arm electrode is attached to the second left parasternal intercostal space, and the left leg electrode is attached to the tip of the scapula. The vector directions in these modified leads are as follows: I_M – electrode 1 as the negative pole and electrode 2 as the positive pole, II_M – electrode 1 as the negative pole and electrode 3 as the positive pole, and III_M – electrode 2 as the negative pole and electrode 3 as the positive pole.

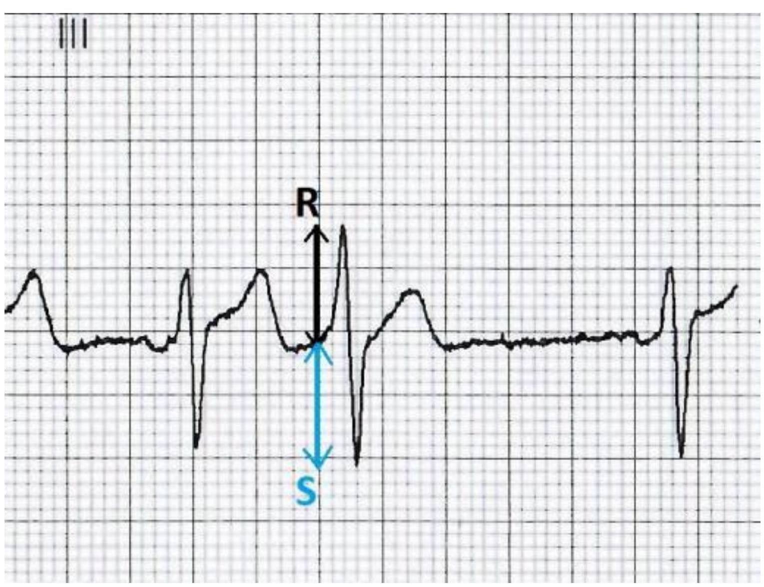

Figure 2: The image depicts the R wave (black arrow) and S wave (blue arrow) of a premature ventricular contraction.

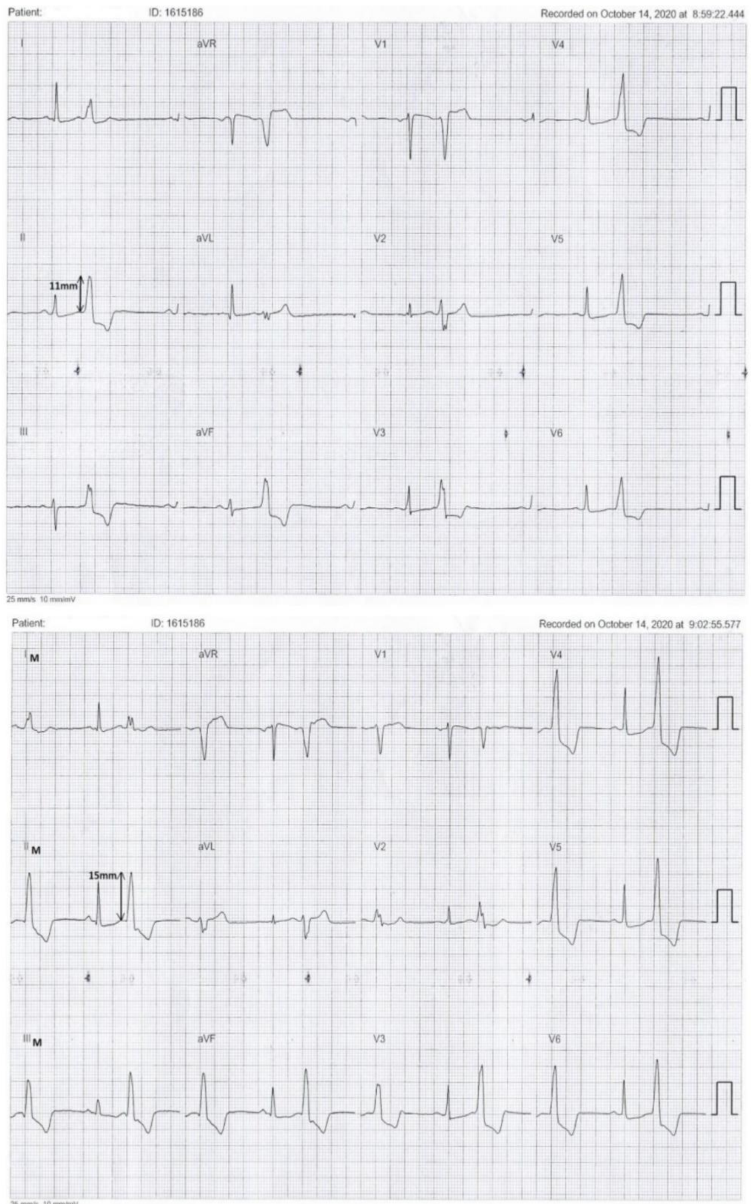

Figure 3: The standard electrocardiogram shows a PVC with a left bundle branch block morphology in the inferior axis and the precordial transition zone between leads V_2 and V_3. Given the broad initial r wave in V_2 and the early precordial transition zone, the premature ventricular contractions (PVCs) may first be considered to have arisen from the left ventricular outflow tract. The tall R wave in modified leads II and III indicate the origin of the PVCs from the right ventricular outflow tract (RVOT). However, the II_{MR}/II_{CR} is 1.36 (15/11), which is in favor of a PVC origin from the RVOT. The PVCs were successfully ablated from the RVOT (-30 ms pre-QRS).

RESULTS

The present study recruited 102 patients at a mean age of 44.32±13.77 years, with a minimum of 18 years and a maximum of 71 years. Half the patients were in the age range of 35 to 55 years. Fifty-two percent of the patients were male. The mean LVEF was 44.44±12.92%. In the electrophysiology study, RVOT PVCs were seen in 48% of the patients and LVOT PVCs in 52%.

The voltages of the R and S waves in the conventional and modified leads are presented in Table 1. Concerning the defined notching in the method section, the presence or absence of notching was evaluated in all the leads (Table 2).

Table 1: Mean voltage of the R and S waves of PVCs in the modified and conventional leads in millimeter

		Conventional	Modified
I	R wave	1.9±2.54	2.14±3.09
	S wave	2.39±2.55	5.62±4.13
II	R wave	16.40±5.02	10.63±6.43
	S wave	0.02±0.29	0.77±1.49
III	R wave	16.58±6.13	14.32±7.76
	S wave	0	1.35±2.66

PVC, Premature ventricular contraction

Table 2: Presence or absence of notching in the modified (M) and conventional (C) leads

Lead	With Notching (%)	Without Notching (%)
I_M	35(34.3)	67(65.7)
I_C	50(49)	52(51)
II_M	36(35.3)	66(64.7)
II_C	11(10.8)	91(89.2)
III_M	36(35.3)	66(64.7)
III_C	20(19.6)	82(80.4)

For the assessment of the relationship between continuous variables and PVC origins, an independent sample *t* test was used (Table 3). No relationship was seen between sex and the origin of PVCs (*P*=0.329). As was mentioned previously, we compared the voltage of the R and S waves in the modified and conventional leads using simple formulas. All the formulas (Table 3) had significant *P* values concerning the origins of PVCs except the I_{MR}/I_{CR} and $I_{MR\text{-}S}/I_{CR\text{-}S}$ formulas.

For the assessment of the diagnostic value of these formulas in localizing RVOT and the LVOT PVCs by comparison with the electrophysiology study (as the gold standard), a cutoff was determined using the ROC curve. Based on the determined cutoff, sensitivity, specificity, the negative predictive value (NPV), and the positive predictive value (PPV) were calculated. For instance, for the $III_{MR}\text{-}III_{MS}/III_{CR}\text{-}III_{CS}$ formula, we calculated an AUC of 0.877 with a *P* value of 0.001 (95% CI, 0.811 to 0.943). The proportion of the R and S waves of PVCs in modified Lead III to conventional lead III at a cutoff of 0.744 had a sensitivity of 0.85 and a specificity of 0.80. Other sensitivity and specificities and their cutoffs are presented in Table 4.

The relationships between notching presence in the modified leads and the origins of PVCs were analyzed using the χ^2 test (Table 5).

In 62 patients (93.9%) without notching in lead II, RFCA was successful (*P*=0.001). However, the presence or absence of notching in leads I and III had no relationship with RFCA success (*P*=0.093 and *P*=0.113, respectively).

Table 3: Relationships between continuous variables and the origins of PVCs

Difference and Proportion	RVOT	LVOT	*P* value
Age (y)	39.65±13.1	48.77±12.95	0.001
LVEF (%)	49.38±10.03	39.87±13.67	0.0001
$I_{MR\text{-}CR}$ *	-0.66±3.02	1.08±3.35	0.007
$II_{MR\text{-}CR}$	-0.47±6.35	-10.65±6.52	0.0001
$III_{MR\text{-}CR}$	4.51±8.37	-8.51±8.51	0.0001
$I_{MS\text{-}CS}$	5.32±4.70	1.29±3.68	0.0001
$II_{MS\text{-}CS}$	0.08±0.57	1.36±1.87	0.0001
$III_{MS\text{-}CS}$	0.59±0.82	2.06±3.47	0.004
I_{MR}/I_{CR}	**0.66±0.65**	**1.25±1.47**	**0.069**
II_{MR}/II_{CR}	1.04±0.56	0.40±0.31	0.0001
III_{MR}/III_{CR}	1.55±1.31	0.62±0.50	0.0001
I_{MS}/I_{CS}	3.14±2.58	1.60±1.75	0.001
$(IM_{R\text{-}S})/(IC_{R\text{-}S})$	**-0.56±4.74**	**0.30±2.46**	**0.271**
$(IIM_{R\text{-}S})/(IIC_{R\text{-}S})$	1.04±0.55	0.30±0.40	0.0001
$(IIIM_{R\text{-}S})/(IIIC_{R\text{-}S})$	1.50±1.22	0.47±0.48	0.0001

*All the measurements in the equations are in millimeter.
**M, Modified; C, Conventional; R, R wave; S, S wave; RVOT, Right ventricular outflow tract; LVOT, Left ventricular outflow tract; PVC, Premature ventricular contraction

Table 4: Sensitivity, specificity, PPV, and NPV of continuous variables for PVC origin prediction based on changed lead placement used in this study

Continuous Variables	AUC (95% CI)	Cutoff	Sen.	Spec.	PPV	NPV
Age*	0.30(0.20-0.41)	39.5	49	25	38	34
LVEF**	0.73(0.64-0.83)	41.2	83	50	60	76
$I_{MR}-I_{CR}$	0.32(0.22-0.43)	- 0.75	63	20	42	37
$II_{MR}-II_{CR}$	**0.87(0.80-0.93)**	**-6.5**	**85**	**74**	**75**	**85**
$III_{MR}-III_{CR}$	**0.86(0.79-0.93)**	**-1.25**	**82**	**81**	**80**	**82**
$I_{MS}-I_{CS}$	0.75(0.65-0.85)	3.25	71	78	74	74
$II_{MS}-II_{CS}$	0.31(0.21-0.42)	0.25	19	57	25	41
$III_{MS}-III_{CS}$	0.40(0.29-0.51)	0.75	36	53	41	47
I_{MR}/I_{CR}	0.35(0.21-0.50)	0.31	70	27	52	43
II_{MR}/II_{CR}	**0.88(0.81-0.94)**	**0.59**	**90**	**76**	**22**	**88**
III_{MR}/III_{CR}	**0.86(0.79-0.93)**	**0.87**	**84**	**80**	**78**	**84**
I_{MS}/I_{CS}	0.69(0.55-0.83)	1.46	74	65	60	77
$(I_{MR}-I_{MS})/(I_{CR}-I_{CS})$	0.43(0.31-0.56)	0.1	45	30	36	37
$(II_{MR}-II_{MS})/(II_{CR}-II_{CS})$	**0.89(0.83-0.95)**	**0.54**	**91**	**74**	**76**	**91**
$(III_{MR}-III_{MS})/(III_{CR}-III_{CS})$	**0.87(0.81-0.94)**	**0.74**	**85**	**80**	**80**	**85**

PPV, Positive predictive value; NPV, Negative predictive value; AUC, Area under the curve; PVC, Premature ventricular contraction

Table 5: Relationships between notching presence in the modified leads and PVC origins

Lead	RVOT	LVOT	*P* value
I_M	4 (8.2%)	31 (58.5%)	0.0001
II_M	2 (4.1%)	34 (64.2%)	0.0001
III_M	3 (6.1%)	33 (62.3%)	0.0001
I_C	26 (53.1 %)	24 (45.3 %)	0.432
II_C	5 (10.2%)	6 (11.3%)	0.856
III_C	10 (20.4%)	10 (18.9 %)	0.845

RVOT, Right ventricular outflow tract; LVOT, Left ventricular outflow tract; PVC, Premature ventricular contraction

DISCUSSION

Multiple methods have been presented to localize the origins of PVCs. Some of these methods are complicated by the use of sophisticated diagnostic tools such as computed tomography (CT) scanning, magnetic resonance imaging, and convolutional neural networks, which may not be available in some areas. In addition, some of the previously introduced methods utilize difficult formulas that may be cumbersome in overcrowded electrophysiological labs. In the current novel study, we sought to show that a simple electrode placement change could yield valuable information regarding the origins of PVCs and the probability of their successful ablation.

Our results demonstrated that patients with LVOT PVCs were older and had lower LVEF values than patients with RVOT PVCs. Our comparison of the voltages of the R and S waves of these modified leads (the difference and proportion) with the same-named leads (conventional) placed at the lower level showed that the voltage of the R wave in LVOT PVCs decreased significantly compared with that in RVOT PVCs in modified leads II and III (Table 3). In addition, PVCs originating from the sub valve and aortomitral continuity in modified leads II and III had a deeper S wave than PVCs originating from the aortic cusps and the LV summit.

Our formulas II_{MR-CR} and III_{MR-CR} show that we subtract the height of the PVC R wave in the modified and conventional leads from each other. According to our results, the height of the R wave in RVOT PVCs increased in lead III significantly compared with that in conventional lead placement, whereas no such change occurred in LVOT PVCs, likely due to the increased distance of the modified leads from the LVOT by comparison with the RVOT. Other formulas for the comparison of R and S waves in the modified and conventional lead placements are presented in Table 3. Formulas I_{MR}/I_{CR} and I_{MR-S}/I_{CR-S} failed to differentiate between RVOT and LVOT PVCs, while the other formulas were helpful.

Best sensitivity and specificity were achieved in the comparison of (the difference and proportion) of the R waves of PVCs in modified and conventional leads II and III. As is presented in Table 3, the use of formulas II_{MR}/II_{CR}, II_{MR}-II_{MS}/II_{CR}-II_{CS}, and III_{MR}-III_{MS}/III_{CR}-III_{CS} resulted in the best sensitivity and specificity (85–74, 91–74, and 85–80, respectively) to differentiate between RVOT and LVOT PVCs.

The presence or absence of notching was another factor that we assessed. The presence of notching was related to LVOT PVCs, likely in consequence of the distance between the LVOT to lead placement compared with the RVOT or velocity reduction in deeper structures. It is worth noting that the absence of notching in modified lead II was accompanied by the greater success rate of PVC ablation.

CONCLUSIONS

The easy novel limb electrode placement system introduced herein can help us achieve a better understanding of the origins of IOT-PVCs. Comparison of the R and S waves of PVCs in modified leads II and III with the same-named conventional leads can yield the best results based on our findings. The most useful formulas concerning the sensitivity and specificity in our study are as follows: II_{MR}/II_{CR}, III_{MR}/III_{CR}, II_{MR}-II_{MS}/II_{CR}-II_{CS}, and III_{MR}-III_{MS}/III_{CR}-III_{CS}. The absence of notching at modified lead II can be a predictor of successful PVC ablation.

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